RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1-74 were initially filed. Claims 33-74 have been withdrawn from consideration as directed to non-elected subject matter. Claim 3 was canceled without prejudice or disclaimer in the previous response. Claims 1, 2, 4, 7, 13, and 22 have been amended. No new matter is added by the amendments. Claims 1-2 and 4-32 are currently pending in the application and presented herein for reconsideration.

B. Rejection Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 1-32 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out the subject matter which Applicant regards as the invention. In particular, the Action asserts that the meaning of the term "capable of" cannot be ascertained in claims 1-32.

In response, Applicants note that the recited term has been amended or deleted in claims 1, 2, 4, 7, 13, and 22 in order to advance the prosecution of the case and because the amendments do not narrow the scope of the claims. Specifically, the term "capable of" as is it used in the claims is inherent in the limitations recited in the original claims. Thus Applicants do not disclaim any subject matter through the amendment. It is believed that the rejection is moot in light of the amendments.

In view of the foregoing it is respectfully submitted that the claims are fully definite and removal of the rejection is thus requested.

C. **Rejection Under 35 U.S.C. §102**

The Action rejects claims 1, 3, 5-9, 14-16, 18-21 and 29 under 35 U.S.C. §102(e) as allegedly anticipated by Hultgren *et al.* (US Patent No. 6,001,823). Applicants respectfully traverse as the cited reference does not teach the claim limitations. Current claim 1 of the instant case, upon which each of the remaining rejected claims depends, reads as follows:

> 1. (Currently amended) A method of obtaining a bacterium comprising a nucleic acid sequence encoding a binding protein capable of binding a target ligand comprising the steps of:
> (a) providing a Gram negative bacterium comprising a nucleic acid sequence encoding a candidate binding protein, wherein said binding protein is expressed in soluble form in the periplasm of said bacterium;
> (b) contacting said bacterium with a labeled ligand that diffuses into said periplasm; and
> (c) selecting said bacterium based on the presence of said labeled ligand within the periplasm, wherein said ligand and said candidate binding protein are bound in said bacterium.

The Action has not shown teachings in the cited reference demonstrating either of steps (b) or (c), nor a basis for concluding that such steps are suggested by the reference. For example, step (b) requires contacting the bacterium from step (a) with a labeled ligand. Hultgren *et al.* does not teach this step. Rather, Hultgren involves first contacting an **isolate of proteins with a labeled ligand,** and second, contacting a **bacteria with an unlabeled ligand,** but not contacting a **bacteria with a labeled ligand** as recited in step (b). For example, the assay described in column 14 that uses a "fluorescence labeled variant" is described in Example 10, column 84 of the Hultgren patent to contact a "purification" of protein with the labeled variant. The cited reference therefore does not teach or suggest contacting a bacterium with the labeled variant either here or elsewhere. Furthermore, the assay described in columns 10 and 11 of the Hultgren patent recites contacting bacteria with a "substance." This substance is defined in columns 6 and 7 as a compound with the effect of "prevention, inhibition, or enhancement of binding between

the pilus subunits and a periplasmic molecular chaperone." The Hultgren patent does not teach or suggest that the substance used to contact the bacterium is a labeled ligand. Because the reference teaches first contacting an **isolate of proteins** with a labeled ligand, and second, contacting a bacterium with an **unlabeled ligand**, but not contacting a bacterium with a **labeled** ligand, there is no teaching in the cited reference of step (b) of claim 1, and the claim cannot be anticipated.

Similarly, step (c) of claim 1 entails "selecting said bacterium based on the presence of said labeled ligand within the bacterium." Hultgren *et al.* also does not teach this step. Rather, Hultgren teaches a method for selecting a **substance** based on **comparing growth rates** within a sample of bacteria, not a method for selecting a **bacterium** from a sample based on the **presence of labeled ligand within the bacterium** as recited in step (c). For example, the assays described in columns 10-12 of the Hultgren patent recite methods for "testing a candidate substance... by determination of the growth rate of the bacteria." The cited reference teaches the determination of growth rate as follows:

> By counting of colonies on solid agar plates striped with the bacteria, by counting bacterial density in liquid growth media (OD_{600} determination), by measuring fluorescence of substances such as NAD(P)H, ATP, or amino acids, which are contained in the bacterial cells only, or by any other convenient detection system known to the person skilled in the art.

The foregoing does not teach detection of a labeled ligand as the substances detected are native to the bacterial cells themselves. Specifically, the reference teaches measuring fluorescence of substances that are unlabeled and "contained in the bacterial cells." Labeled ligands are neither contained in bacterial cells nor are bacterial cells labeled under Hultgren. Therefore, the reference fails to teach the determination of growth rate based on the presence of a labeled ligand. Additionally, Hultgren teaches measuring fluorescence or using "any other convenient detection system known to the person skilled in the art" for "the determination of

growth rate" and "identifying the substance as potentially therapeutic," and does not teach measuring fluorescence or the using any convenient detection systems for **selecting a bacterium** based on the presence of a labeled ligand as recited in step (c). Furthermore, as is discussed in the preceding paragraph, since Hultgren *et al.* fails to teach contacting bacteria with a labeled ligand, the reference necessarily fails to teach selection of a bacteria "based on the presence of said labeled ligand within the periplasm." Because no teaching in Hultgren *et al.* has been shown for selecting a bacterium based on the presence of a labeled ligand, there is no teaching in the cited reference of step (c) of claim 1, and the claim cannot be anticipated.

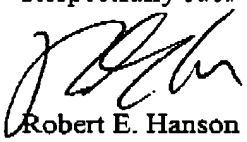
Applicants further note that the cited reference does not suggest the claimed method as Hultgren is directed towards obtaining a therapeutic substance, not obtaining a bacterium encoding a binding protein as recited in claim 1. For example, the Hultgren patent teaches the identification of a potentially therapeutic substance, and does not teach that the selection of a bacterium will identify whether a substance is potentially therapeutic. Therefore, the Hultgren patent would not suggest or motivate one with skill in the art to select a bacterium as recited in step (c). Similarly, Hultgren teaches that the identification of a substance as potentially therapeutic is accomplished by determination of growth rate, which would not be accomplished by contacting a bacterium with a labeled ligand. Therefore, the Hultgren patent does not suggest or motivate a person with skill in the art to contact a bacterium with a labeled ligand as recited in step (b), or to select a bacterium based on the presence of a labeled ligand as recited in step (c). Because no teaching in Hultgren *et. al.* teaches, suggests or motivates a person with skill in the art to practice step (b) or step (c) of claim 1, the claims cannot be anticipated or rendered obvious by the cited reference.

In view of the foregoing removal of the rejection is respectfully requested.

D. Conclusion

In light of the foregoing, applicants submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned at (512) 536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: March 2, 2005